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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/525,710	02/24/2005	Burkhard Kroger	13111-00006-US	3746
23416 7590 05/14/2007 CONNOLLY BOVE LODGE & HUTZ, LLP P O BOX 2207 WILMINGTON, DE 19899			EXAMINER SAIDHA, TEKCHAND	
			ART UNIT 1652	PAPER NUMBER
			MAIL DATE 05/14/2007	DELIVERY MODE PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary

Application No.

10/525,710

Applicant(s)

KROGER ET AL.

Examiner

Tekchand Saidha

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1652

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 11 April 2007.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-16 is/are pending in the application.
- 4a) Of the above claim(s) 15 and 16 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-14 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 24 February 2005 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☒ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date 2/24/05 & 12/5/05.
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____.
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: _____.

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DETAILED ACTION

1. Applicant's election with traverse of Group I (claims 1-14, SEQ ID NO: 3 from *Mycobacterium tuberculosis*) in reply filed April 11, 2007 is acknowledged. The traversal is on the ground(s) that there is no undue burden on the Examiner to search this invention.

The traversal is unclear regarding the burden to search which groups or species. Perhaps Applicants meant search and examination of all the groups and sequences will not be undue burden to the Examiner. Should this be the case Applicants' argument is not found persuasive because depending upon the restricted group (I or II) and the sequence (SEQ ID NO:?) being examined, separate additional searches will be required. In cases such as the present one where descriptive sequence information is provided, the sequences are searched in appropriate databases. Each additional sequence will involve searching the additional sequence in different databases such as US Patent data bases for issued patent, published applications & pending applications; Genbank/protein data base among others, and searching for one sequence will not necessarily find art for the other sequence(s). Searching, therefore is not coextensive. There is search burden also in the non-patent literature. This additional searching as explained above would therefore involve undue burden to the Examiner. The requirement is still deemed proper and is therefore made FINAL.

2. **Claims withdrawn** :

Claims 15-16 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

3.

Priority

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Acknowledgment is made of applicants' claim for priority based on an application filed in Germany on 08/26/2002.

4. ***Drawings***

Drawings filed on 2/24/05 are acceptable for examination purposes.

5. ***Specification***

The specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors of which applicant may become aware in the specification.

6. ***Claim Objections***

Claims 4, 5, 6 are objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. These claims include non-elected subject matter which must be deleted to overcome this objection.

7. ***Claim Rejections - 35 USC § 112*** (first paragraph)

Written Description

Claims 1-4 and 7-14 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. These claims are directed to a method of fermentative production of at least one sulfur containing fine chemical (or compound) which comprises fermenting a coryneform bacteria, wherein the coryneform bacteria expresses at least one heterologous nucleotide sequence which codes for a protein with

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O-acetylhomoserine sulfhydrylase (metY) activity, wherein the DNA (or polynucleotide) is a genus of DNA from any source and having no defined structure.

The specification does not contain any disclosure or description of the structure and function of all DNA sequences from any source that are capable of encoding a protein with O-acetylhomoserine sulfhydrylase (metY) activity. The specification discloses the DNA sequences of SEQ ID No. 1, 3, 5, 7..... 51 & 53 (See claim 5 and specification, page 3) encoding a protein with O-acetylhomoserine sulfhydrylase (metY) activity of the claimed genus which is insufficient to put one of skill in the art in possession of the attributes and features of all species within the claimed genus, which may also include species hitherto undiscovered. Therefore, one skilled in the art cannot reasonably conclude that the applicant had possession of the claimed invention at the time the instant application was filed.

8. ***Enablement Rejection***

Claims 1-4 and 7-14 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of fermentative production of methionine which comprises fermenting a coryneform bacteria, wherein the coryneform bacteria expresses at least one heterologous polynucleotide sequence of SEQ ID NO: 3, encoding a protein with O-acetylhomoserine sulfhydrylase (metY) activity of sequence of SEQ ID NO: 4, does not reasonably provide enablement for any polynucleotide encoding a protein with O-acetylhomoserine sulfhydrylase (metY) activity (claim 1) or claims dependent thereof. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly

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connected, to make the invention commensurate in scope with these claims.

The scope of the claims does not commensurate with the enablement provided by the disclosure with regard to the extremely large number of polynucleotides broadly encompassed by the claims including variants or mutants. Since the amino acid sequence of a protein determines its structural and functional properties, predictability of which changes can be tolerated in a protein's amino acid sequence and obtain the desired activity requires a knowledge of and guidance with regard to which amino acids in the protein's sequence, if any, are tolerant of modification and which are conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the ways in which the proteins' structure relates to its function. However, in this case the disclosure is limited to the nucleotide sequences of SEQ ID NO: 1, 3, 5, 7,51 & 53 and encoded amino acid sequences of SEQ ID NO : 2, 4, 6,52 & 54, respectively.

While recombinant and mutagenesis techniques are known, it is not routine in the art to screen for multiple substitutions or multiple modifications, as encompassed by the instant claims, and the positions within a protein's sequence where amino acid modifications can be made with a reasonable expectation of success in obtaining the desired activity/utility are limited in any protein and the result of such modifications is unpredictable. In addition, one skilled in the art would expect any tolerance to modification for a given protein to diminish with each further and additional modification, e.g. multiple substitutions.

The specification does not support the broad scope of the method claims which encompass using DNA comprising all

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modifications of DNA of SEQ ID NO: 3 or a DNA encoding a protein with O-acetylhomoserine sulfhydrolase (metY) activity because the specification does not establish: (A) regions of the protein structure which may be modified without effecting O-acetylhomoserine sulfhydrolase (metY) activity; (B) the general tolerance of O-acetylhomoserine sulfhydrolase (metY) to modification and extent of such tolerance; (C) a rational and predictable scheme for modifying any O-acetylhomoserine sulfhydrolase (metY) residues with an expectation of obtaining the desired enzymatic or biological function; and (D) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims. The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of exact nature of the encoding DNA (or polynucleotide) encoding a specific O-acetylhomoserine sulfhydrolase (metY) activity of known substrate specificity having the desired enzymatic characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

9. ***Claim Rejections - 35 USC § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

Claims 1-3, 7-14 are rejected under 35 U.S.C. 102(a) as being anticipated by any one of the following Degussa's references: (1) WO 02/18613 A, (Degussa), March 7, 2002]; WO 02/10206 A (Degussa), February 7, 2002] or [WO 02/10209 A, (Degussa), February 7, 2002].

Degussa discloses the production of 'sulfur-containing fine chemical' by fermentative preparation using metY gene coding for O-acetyl-L-homoserine sulfhydrylase from *Corynebacterium glutamicum* 13032 (see page 6, line 22) is present in enhanced form or is over-expressed, varying copy number, replicated, integrated and amplified in the chromosome (See abstract; page 11, lines 5-10, 30-35). The reference also uses other polynucleotides (which are at least 70% identical) encoding the O-acetyl-L-homoserine sulfhydrylase of SEQ ID NO: 2. These polynucleotides (or DNA) from other sources which are at least 70% identical are considered heterologous (See pages 2-4). Suitable strains of *Corynebacterium* (ATCC 13032) or *Brevibacterium* used for making L-methionine are listed on page 6-7, for example. The reference on pages 13-15 further describe increased L-lysine and/or L-methionine production by enhancement

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of one or more genes selected from a group consisting of *gap* gene which codes for glyceraldehydes 3-phosphate dehydrogenase; *pgk* gene which codes for 3-phosphoglycerate kinase; *pyc* gene (pyruvate carboxylase); *lysC* gene; *metA* (homoserine O-acetyltransferase) (page 10, lines 27-30), among several others. Method for the preparation of animal feed additive comprising L-methionine using the fermentation of the L-methionine by *Corynebacterium* bacteria are also taught by the reference (See for example, claims 25 & 38-39). The reference is anticipatory for teaching all the limitations of the claims.

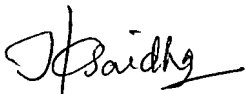
10. No claim is allowed.

11. Method claims drawn to SEQ ID NO: 3 is free of prior art.

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Tekchand Saidha whose telephone number is (571) 272 0940. The examiner can normally be reached on 8.30 am - 5.00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapu Achutamurthy can be reached on (571) 272 0928. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.



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May 7, 2007